

WHAT IS CLAIMED IS:

1. A method of inducing or accelerating a healing process of a skin wound, the method comprising the step of administering to the skin wound a therapeutically effective amount of insulin and at least one additional agent acting in synergy with said insulin to induce or accelerate the healing process of the skin wound.
2. The method of claim 1, wherein said administering is effected by a single application.
3. The method of claim 1, wherein said therapeutically effective amount of insulin has an insulin concentration ranging from 0.1 μ M to 10 μ M.
4. The method of claim 4, wherein said at least one additional agent is a platelet-derived growth factor.
5. The method of claim 1, wherein said at least one additional agent is a PKC- α inhibitor.
6. The method of claim 1, wherein said wound is selected from the group consisting of an ulcer, a burn, a laceration and a surgical incision.
7. The method of claim 6, wherein said ulcer is a diabetic ulcer.
8. The method of claim 1, wherein said insulin is recombinant.
9. The method of claim 1, wherein said insulin is of a natural source.
10. The method of claim 1, wherein said insulin and at least one additional agent are contained in a pharmaceutical composition adapted for topical application.

11. The method of claim 10, wherein said pharmaceutical composition is selected from the group consisting of an aqueous solution, a gel, a cream, a paste, a lotion, a spray, a suspension, a powder, a dispersion, a salve and an ointment.

12. The method of claim 10, wherein said pharmaceutical composition includes a solid support.

13. A method of inducing or accelerating a healing process of a skin wound, the method comprising the step of implanting into the skin wound a therapeutically effective amount of insulin secreting cells, so as to induce or accelerate the healing process of the skin wound.

14. The method of claim 13, wherein said wound is selected from the group consisting of an ulcer, a burn, a laceration and a surgical incision.

15. The method of claim 14, wherein said ulcer is a diabetic ulcer.

16. The method of claim 13, wherein said cells are transformed to produce and secrete insulin.

17. The method of claim 16, wherein said cells are transformed by a recombinant PDX1 gene and therefore said cells produce and secrete natural insulin.

18. The method of claim 16, wherein said cells are transformed by a cis-acting element sequence integrated upstream to an endogenous insulin gene of said cells and therefore said cells produce and secrete natural insulin.

19. The method of claim 16, wherein said cells are transformed by a recombinant insulin gene and therefore said cells produce and secrete recombinant insulin.

20. The method of claim 13, wherein said insulin secreting cells are capable of forming secretory granules.

21. The method of claim 13, wherein said insulin secreting cells are endocrine cells.

22. The method of claim 13, wherein said insulin secreting cells are of a human source.

23. The method of claim 13, wherein said insulin secreting cells are of a histocompatibility humanized animal source.

24. The method of claim 13, wherein said insulin secreting cells secrete human insulin.

25. The method of claim 13, wherein said insulin secreting cells are autologous cells.

26. The method of claim 13, wherein said cells are selected from the group consisting of fibroblasts, epithelial cells and keratinocytes.

27. A method of inducing or accelerating a healing process of a skin wound, the method comprising the step of transforming cells of the skin wound to produce and secrete insulin, so as to induce or accelerate the healing process of the skin wound.

28. The method of claim 27, wherein said wound is selected from the group consisting of an ulcer, a burn, a laceration and a surgical incision

29. The method of claim 28, wherein said ulcer is a diabetic ulcer.

30. The method of claim 27, wherein said cells are transformed by a recombinant PDX1 gene and therefore said cells produce and secrete natural insulin.

31. The method of claim 27, wherein said cells are transformed by a cis-acting element sequence integrated upstream to an endogenous insulin gene of said cells and therefore said cells produce and secrete natural insulin.

32. The method of claim 27, wherein said cells are transformed by a recombinant insulin gene and therefore said cells produce and secrete recombinant insulin.

33. A method of inducing or accelerating a healing process of a skin wound, the method comprising the step of transforming cells of said skin wound to produce a protein kinase C, so as to induce or accelerate the healing process of the skin wound.

34. The method of claim 33, wherein said skin wound is selected from the group consisting of an ulcer, a burn, a laceration and a surgical incision

35. The method of claim 34, wherein said ulcer is a diabetic ulcer.

36. The method of claim 33, wherein said cells are transformed to produce a protein kinase C transcription activator and therefore said cells produce natural protein kinase C.

37. The method of claim 33, wherein said cells are transformed by a cis-acting element sequence integrated upstream to an endogenous protein kinase C of said cells and therefore said cells produce natural protein kinase C.

38. The method of claim 33, wherein said cells are transformed by a recombinant protein kinase C gene and therefore said cells produce recombinant protein kinase C.

39. The method of claim 33, wherein said protein kinase C is selected from the group consisting of PKC- β 1, PKC- β 2, PKC- γ , PKC- θ , PKC- λ , and PKC- ι .

40. The method of claim 33, wherein said protein kinase C is selected from the group consisting of PKC- α , PKC- δ , PKC- ϵ , PKC- η and PKC- ζ .

41. A pharmaceutical composition for inducing or accelerating a healing process of a skin wound, the pharmaceutical composition comprising, as an active ingredient, a therapeutically effective amount of insulin and at least one additional agent acting in synergy with said insulin, and a pharmaceutically acceptable carrier being designed for topical application of the pharmaceutical composition.

42. The pharmaceutical composition of claim 41, wherein said at least one additional agent is a growth factor.

43. The pharmaceutical composition of claim 42, wherein said growth factor is a platelet-derived growth factor.

44. The pharmaceutical composition of claim 41, wherein said at least one additional agent is a PKC- α inhibitor.

45. The pharmaceutical composition of claim 41, wherein said insulin is a recombinant.

46. The pharmaceutical composition of claim 41, wherein said insulin is of a natural source.

47. The pharmaceutical composition of claim 41, wherein said wound is selected from the group consisting of an ulcer, a burn, a laceration and a surgical incision.

48. The pharmaceutical composition of claim 41, wherein said ulcer is a diabetic ulcer.

49. The pharmaceutical composition of claim 41, wherein said insulin and at least one additional agent is contained in a formulation adapted for topical application.

50. The pharmaceutical composition of claim 49, wherein said formulation is selected from the group consisting of an aqueous solution, a gel, a cream, a paste, a lotion, a spray, a suspension, a powder, a dispersion, a salve and an ointment.

51. The pharmaceutical composition of claim 50, wherein said pharmaceutical composition includes a solid support.

52. A pharmaceutical composition for inducing or accelerating a healing process of a skin wound, the pharmaceutical composition comprising, as an active ingredient, insulin secreting cells, and a pharmaceutically acceptable carrier being designed for topical application of the pharmaceutical composition.

53. The pharmaceutical composition of claim 52, wherein said wound is selected from the group consisting of an ulcer, a burn, a laceration and a surgical incision.

54. The pharmaceutical composition of claim 53, wherein said ulcer is a diabetic ulcer.

55. The pharmaceutical composition of claim 52, wherein said cells are transformed to produce and secrete insulin.

56. The pharmaceutical composition of claim 52, wherein said cells are transformed by a recombinant PDX1 gene and therefore said cells produce and secrete natural insulin.

57. The pharmaceutical composition of claim 52, wherein said cells are transformed by a cis-acting element sequence integrated upstream to an endogenous insulin gene of said cells and therefore said cells produce and secrete natural insulin.

58. The pharmaceutical composition of claim 52, wherein said cells are transformed by a recombinant insulin gene and therefore said cells produce and secrete recombinant insulin.

59. The pharmaceutical composition of claim 52, wherein said insulin secreting cells are capable of forming secretory granules.

60. The pharmaceutical composition of claim 52, wherein said insulin secreting cells are endocrine cells.

61. The pharmaceutical composition of claim 52, wherein said insulin secreting cells are of a human source.

62. The pharmaceutical composition of claim 52, wherein said insulin secreting cells are of a histocompatibility humanized animal source.

63. The pharmaceutical composition of claim 52, wherein said insulin secreting cells secrete human insulin.

64. The pharmaceutical composition of claim 52, wherein said insulin secreting cells are autologous cells.

65. The pharmaceutical composition of claim 52, wherein said cells are selected from the group consisting of fibroblasts, epithelial cells and keratinocytes.

66. A pharmaceutical composition for inducing or accelerating a healing process of a skin wound, the pharmaceutical composition comprising, as an active ingredient, a nucleic acid construct being designed for transforming cells of said skin

wound to produce and secrete insulin, and a pharmaceutically acceptable carrier being designed for topical application of the pharmaceutical composition.

67. The pharmaceutical composition of claim 66, wherein said wound is selected from the group consisting of an ulcer, a burn, a laceration and a surgical incision

68. The pharmaceutical composition of claim 67, wherein said ulcer is a diabetic ulcer.

69. The pharmaceutical composition of claim 66, wherein said cells are transformed by a recombinant PDX1 gene and therefore said cells produce and secrete natural insulin.

70. The pharmaceutical composition of claim 66, wherein said cells are transformed by a cis-acting element sequence integrated upstream to an endogenous insulin gene of said cells and therefore said cells produce and secrete natural insulin.

71. The pharmaceutical composition of claim 66, wherein said cells are transformed by a recombinant insulin gene and therefore said cells produce and secrete recombinant insulin.

72. A pharmaceutical composition for inducing or accelerating a healing process of a skin wound, the pharmaceutical composition comprising, as an active ingredient, a nucleic acid construct being designed for transforming cells of said skin wound to produce a protein kinase C, and a pharmaceutically acceptable carrier being designed for topical application of the pharmaceutical composition.

73. The pharmaceutical composition of claim 72, wherein said skin wound is selected from the group consisting of an ulcer, a burn, a laceration and a surgical incision

74. The pharmaceutical composition of claim 73, wherein said ulcer is a diabetic ulcer.

75. The pharmaceutical composition of claim 72, wherein said cells are transformed to produce a protein kinase C transcription activator and therefore said cells produce natural protein kinase C.

76. The pharmaceutical composition of claim 72, wherein said cells are transformed by a cis-acting element sequence integrated upstream to an endogenous protein kinase C of said cells and therefore said cells produce natural protein kinase C.

77. The pharmaceutical composition of claim 72, wherein said cells are transformed by a recombinant protein kinase C gene and therefore said cells produce recombinant protein kinase C.

78. The pharmaceutical composition of claim 72, wherein said protein kinase C is selected from the group consisting of PKC- β 1, PKC- β 2, PKC- γ , PKC- θ , PKC- λ , and PKC- ι .

79. The pharmaceutical composition of claim 72, wherein said protein kinase C is selected from the group consisting of PKC- α , PKC- δ , PKC- ϵ , PKC- η and PKC- ζ .

80. A method of inducing or accelerating a healing process of a skin wound, the method comprising the step of administering to the skin wound a therapeutically effective amount of an agent for modulating PKC production and/or activation.

81. A pharmaceutical composition for inducing or accelerating a healing process of a skin wound, the pharmaceutical composition comprising, as an active ingredient, a therapeutically effective amount of an agent for modulating PKC production and/or activation; and a pharmaceutically acceptable carrier.

82. A method of inducing or accelerating a healing process of a skin wound, the method comprising the step of administering to the skin wound a therapeutically effective amount of a PKC activator, so as to induce or accelerate the healing process of the skin wound.

83. A pharmaceutical composition of inducing or accelerating a healing process of a skin wound, the pharmaceutical composition comprising, as an active ingredient, a therapeutically effective amount of a PKC activator, so as to induce or accelerate the healing process of the skin wound, and an acceptable pharmaceutical carrier.

84. A method of inducing or accelerating *ex-vivo* propagation of skin cells, the method comprising the step of subjecting the skin cells to an effective amount of an agent for modulating PKC production.

85. A method of inducing or accelerating a healing process of a skin wound, the method comprising the step of administering to the skin wound a single dose of a therapeutically effective amount of insulin, thereby inducing or accelerating the healing process of said skin wound.

86. The method of claim 85, wherein said skin wound is selected from the group consisting of an ulcer, a burn, a laceration and a surgical incision.

87. The method of claim 86, wherein said ulcer is a diabetic ulcer.

88. The method of claim 85, wherein said insulin is recombinant.

89. The method of claim 85, wherein said insulin is of a natural source.

90. The method of claim 85, wherein said insulin is contained in a pharmaceutical composition adapted for topical application.

91. The method of claim 90, wherein said pharmaceutical composition is selected from the group consisting of an aqueous solution, a gel, a cream, a paste, a lotion, a spray, a suspension, a powder, a dispersion, a salve and an ointment.

92. The method of claim 90, wherein said pharmaceutical composition includes a solid support.

93. A method of inducing or accelerating a healing process of an old skin wound, the method comprising the step of administering to the old skin wound a single dose of a therapeutically effective amount of insulin, thereby inducing or accelerating the healing process of the old skin wound.

94. The method of claim 93, wherein said old skin wound is at least 2 days old.

95. The method of claim 93, wherein said old skin wound is selected from the group consisting of an ulcer, a burn, a laceration and a surgical incision.

96. The method of claim 95, wherein said ulcer is a diabetic ulcer.

97. The method of claim 93, wherein said insulin is recombinant.

98. The method of claim 93, wherein said insulin is of a natural source.

99. The method of claim 93, wherein said insulin is contained in a pharmaceutical composition adapted for topical application.

100. The method of claim 99, wherein said pharmaceutical composition is selected from the group consisting of an aqueous solution, a gel, a cream, a paste, a lotion, a spray, a suspension, a powder, a dispersion, a salve and an ointment.

101. The method of claim 99, wherein said pharmaceutical composition includes a solid support.

102. A pharmaceutical composition for inducing or accelerating a healing process of a skin wound, the pharmaceutical composition comprising, as an active ingredient, a single dose-unit of insulin selected capable of inducing or accelerating a healing process of the skin wound, and a pharmaceutically acceptable carrier being designed for topical application of the pharmaceutical composition.

103. The pharmaceutical composition of claim 102, wherein said single dose-unit of insulin is 0.001 to 5 nM in 0.01 – 0.2 ml of said pharmaceutical composition.

104. The pharmaceutical composition of claim 102, wherein said single dose of insulin is ranging from 0.01 to 0.5 nM in 0.01 – 0.2 ml of said pharmaceutical composition.

105. The pharmaceutical composition of claim 102, wherein said insulin is a recombinant.

106. The pharmaceutical composition of claim 102, wherein said insulin is of a natural source.

107. The pharmaceutical composition of claim 102, wherein said skin wound is selected from the group consisting of an ulcer, a burn, a laceration and a surgical incision.

108. The pharmaceutical composition of claim 102, wherein said ulcer is a diabetic ulcer.

109. The pharmaceutical composition of claim 102, wherein said insulin is contained in a formulation adapted for topical application.

110. The pharmaceutical composition of claim 109, wherein said formulation is selected from the group consisting of an aqueous solution, a gel, a cream, a paste, a lotion, a spray, a suspension, a powder, a dispersion, a salve and an ointment.

111. The pharmaceutical composition of claim 102, wherein said pharmaceutical composition includes a solid support.